

WE CLAIM:

1. A medium molecular weight heparin (MMWH) composition comprising a mixture of sulfated oligosaccharides having molecular weights ranging from about 6,000 Daltons to about 12,000 Daltons.
2. The MMWH composition in accordance with claim 1, wherein said MMWH composition (1) inhibits fibrin-bound thrombin and fluid-phase thrombin by catalyzing antithrombin, and (2) inhibits thrombin generation by catalyzing factor Xa inactivation by antithrombin.
3. The MMWH composition in accordance with claim 1, wherein said MMWH composition has an anti-factor IIa activity of about 40 U/mg to about 100 U/mg, and an anti-factor Xa activity of about 90 U/mg to about 150 U/mg.
4. The MMWH composition in accordance with claim 3, wherein said MMWH composition has an anti-factor IIa activity of about 60 U/mg to about 75 U/mg, and an anti-factor Xa activity of about 100 U/mg to about 125 U/mg.
5. The MMWH composition in accordance with claim 4, wherein said MMWH composition has an anti-factor IIa activity of about 65 U/mg, and an anti-factor Xa activity of about 115 U/mg.
6. The MMWH composition in accordance with claim 1, wherein said MMWH composition comprises a mixture of sulfated oligosaccharides having molecular weights ranging from about 8,000 Daltons to about 10,000 Daltons.
7. The MMWH composition in accordance with claim 1, wherein said MMWH composition has an average molecular weight of about 9,000.
8. The MMWH composition in accordance with claim 1, wherein at least 31% of said sulfated oligosaccharides have a molecular weight greater than or equal to about 7,800.
9. The MMWH composition in accordance with claim 1, wherein at least 25% of said sulfated oligosaccharides have a molecular weight greater than or equal to about 10,000 Daltons.
10. A medium molecular weight heparin (MMWH) composition comprising a mixture of oligosaccharides derived from heparin characterized by one or more of the following characteristics:
 - (a) having antithrombin- and heparin cofactor II (HCII)-related anticoagulant activity *in vitro*;
 - (b) the oligosaccharides are too short to bridge thrombin to fibrin, but are of a sufficient length to bridge antithrombin or HCII to thrombin;
 - (c) having at least 15%, 20%, 25%, 30%, 35%, or 40% oligosaccharides with at least one or more pentasaccharide sequence;
 - (d) enriched for oligosaccharides having a molecular weight range from about 6,000 to about 11,000; 7,000 to 10,000; 7,500 to 10,000; 7,800 to 10,000; 7,800 to 9,800; or 7,800 to 9,600; 8,000 to 9,600;
 - (e) the oligosaccharides have a mean molecular weight of about 7,800 to 10,000, preferably 7,800 to 9,800, more preferably 8,000 to 9,800;
 - (f) at least 30%, 35%, 40%, 45%, or 50% of the oligosaccharides have a molecular weight greater than or equal to 6,000 Daltons, preferably greater than or equal to 8,000 Daltons;
 - (g) a polydispersity of 1.1 to 1.5, preferably 1.2 to 1.4, most preferably 1.3;

(h) having similar anti-factor Xa and anti-factor IIa activities, preferably a ratio of anti-factor Xa activity to anti-factor IIa activity from about 2:1 to about 1:1 and, more preferably, from about 1.5:1 to about 1:1;

5 (i) an anti-factor Xa activity from about 80 IU/mg to about 155 IU/mg, preferably 90 IU/mg to about 130 IU/mg, more preferably, from about 95 IU/mg to about 120 IU/mg and, most preferably 100-110 IU/mg; and

(j) an anti-factor IIa activity from about 20 IU/mg to about 150 IU/mg; preferably 40 IU/mg to about 100 IU/mg, more preferably, from about 80 IU/mg to about 100 IU/mg, most preferably about 90-100 IU/mg.

10 11. A MMWH composition in accordance with claim 10 which has the characteristics of (a), (b), (c) and (d); (a) (b), (c), and (e); (b), (c), (e), and (g); (b), (d), (c), (e), and (h); (b) (c), (d), and (g); (b), (e), (g), (i), and (j); (b), (e), (f), (g), (i) and (j); or (a) through (j).

15 12. A MMWH composition in accordance with claim 10 enriched for oligosaccharides having a molecular weight range of 7,800 to 8,800, preferably 7,800 to 8,600, more preferably 7,800 to 8,500, most preferably 8,000 to 8,500.

13. A MMWH composition in accordance with claim 10 enriched for oligosaccharides having a molecular weight range of 9,000 to 10,000, preferably 9,200 to 9,800, more preferably 9,300 to 9,600, most preferably 9,400 to 9,600.

14. A MMWH composition in accordance with claim 10 comprising oligosaccharides having a mean molecular weight of 7,800 to 8,800, preferably 7,800 to 8,600, more preferably 7,800 to 8,500, most preferably 8,000 to 8,500.

15. A MMWH composition in accordance with claim 10 comprising oligosaccharides having a mean molecular weight of 9,000 to 10,000, preferably 9,200 to 9,800, more preferably 9,300 to 9,600, most preferably 9,400 to 9,600.

16. A MMWH composition as claimed in claim 10, 11, 12, 13, 14, or 15 derived from heparinase depolymerization or nitrous acid depolymerization of unfractionated heparin.

17. A method for treating a thrombotic condition in a subject comprising administering to the subject a pharmacologically acceptable dose of a medium molecular weight heparin (MMWH) composition as claimed in any of the preceding claims.

30 18. The method in accordance with claim 17, wherein said thrombotic condition is arterial thrombosis, coronary artery thrombosis, venous thrombosis, or pulmonary embolism.

19. The method in accordance with claim 17, wherein said MMWH composition is administered by injection.

20. A method of preventing the formation of a thrombus in a subject at risk of developing thrombosis comprising administering to the subject a pharmacologically acceptable dose of a medium molecular weight heparin (MMWH) composition as claimed in any of the preceding claims.

35 21. The method in accordance with claim 20, wherein the subject is at increased risk of developing thrombosis due to a medical condition which disrupts hemostasis.

22. The method in accordance with claim 21, wherein the medical condition is coronary artery disease, or atherosclerosis.

23. The method in accordance with claim 20, wherein the subject is at increased risk of developing thrombosis due to a medical procedure.

24. The method in accordance with claim 23, wherein the medical procedure is cardiac surgery, cardiopulmonary bypass, catheterization, or atherectomy.

5 25. The method in accordance with claim 24, wherein the catheterization is cardiac catheterization

26. A method for inhibiting thrombus formation in a patient comprising the step of administering to the patient a pharmacologically acceptable dose of a medium molecular weight heparin (MMWH) composition as claimed in any of the preceding claims.

10 27. A pharmaceutical composition comprising a MMWH composition as claimed in any of the preceding claims and a pharmaceutically acceptable carrier.

28. A method for treating deep vein thrombosis in a patient comprising administering to a patient undergoing orthopedic surgery a therapeutically effective amount of a MMWH composition as claimed in any of the preceding claims.

15 29. A method for preventing a pulmonary embolism in a subject comprising administering to the subject a therapeutically effective amount of a MMWH composition as claimed in any of the preceding claims.

30. A method for preparing a medium molecular weight heparin (MMWH) composition comprising:

(a) subjecting unfractionated heparin to a limited periodate oxidation reaction such that only the iduronic acids of the unfractionated heparin are oxidized;

(b) subjecting the oxidized unfractionated heparin of step (a) to alkaline hydrolysis; and

(c) recovering said MMWH composition, wherein the MMWH composition comprises a mixture of sulfated oligosaccharides having molecular weights ranging from about 8,000 Daltons to about 12,000 Daltons.

31. Use of a MMWH composition as claimed in any of the preceding claims in the preparation of a medicament for treating a thrombotic condition, or preventing the formation of a thrombus in a subject at risk of developing thrombosis.

32. Use of a MMWH composition as claimed in any of the preceding claims in the preparation of a medicament for inhibiting fibrin-bound thrombin and thrombin generation in a subject.

33. Use of a MMWH composition as claimed in any of the preceding claims in the preparation of a medicament for treating deep vein thrombosis.

30 34. Use of a MMWH composition as claimed in any of the preceding claims in the preparation of a medicament for preventing pulmonary embolism in a subject.

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